



Attorney Docket :
033700WN003

P A T E N T

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:)
)
 D. Scott WILBUR, *et al.*)
)
 U.S. Serial No.: 09/519,998) Examiner: L. Wells
)
 Filed: March 6, 2000) Group Art Unit: 1617

 Title: TRIFUNCTIONAL REAGENT FOR CONJUGATION TO A BIOMOLECULE

DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Declaration of Dr. D. Scott Wilbur

I, Scott Wilbur, declare as follows:

1. I am a Professor of Radiation Oncology at the University of Washington, Radiation Oncology Box 356043, 2121 N. 35th, Room 211, Seattle, Washington, 98195. I am a person of at least ordinary skill in the technical discipline of the present invention. Attached hereto is a copy of my curriculum vitae.
2. I have read U.S. Patent Application No. 09/519,998 entitled "TRIFUNCTIONAL REAGENT FOR CONJUGATION TO A BIOMOLECULE," including the currently

pending claims in that application, claims 1-3, 6-9, 11-22, and 24-39. Additionally, I have read the June 3, 2004, Office Action issued by the United States Patent and Trademark Office relating to this application.

3. I understand that the U.S. Patent and Trademark Office Examiner has rejected claims 1-3, 6-9, 11-22, and 24, 25, and 31-39 as follows:

Claims 1-3, 6-9, 11-22, 24, 25, 31, 21, and 34-39 are rejected under 35 U.S.C. § 103(a) as obvious based on Wilbur et al. (WO 97/29114, published August 14, 1997) in view of Wilbur et al. (*Bioconjugate Chem.* 1997) or Rosenbrough (*J. Pharm. And Exp. Ther.* 1993).

Claim 33 is rejected under 35 U.S.C. § 103(a) as obvious based on Wilbur et al. (WO 97/29114) in view of Wilbur et al. (*Bioconjugate Chem.* 1997) or Rosenbrough in view of Ganosh (U.S. Pat. No. 5,286,850).

I have fully reviewed and understand the cited documents listed above.

4. I understand the Examiner has relied on my international published application Wilbur (WO 97/29114) as the main reference and has essentially interpreted it as teaching all of the features of the claimed reagent except for the incorporation of alpha carboxylate or N-methyl into linker 1. It is also my understanding that the Examiner has interpreted my earlier publication Wilbur (*Bioconjugate Chem.* 1997) as teaching the use of N-methyl and Rosenbrough as teaching the use of alpha carboxylate. Moreover, I understand that the Examiner is of the opinion that by combining the teachings of the above cited documents, the claims are rendered obvious. From a review of the Office Action, it is considered that the Examiner bases this conclusion on the assertion that Wilbur (*Bioconjugate Chem.* 1997)

and Rosenbrough respectively teach that the N-methyl and the alpha carboxylate stabilize biotinimide bonds against enzymatic cleavage.

5. It is my opinion that the paper by Rosebrough (*J. Pharm. And Exp. Ther.* 1993) and my paper (*Bioconjugate Chem.* 1997) fail to adequately teach or suggest the claimed invention. Further, it is unreasonable to think that a person with “ordinary skill in the art” would be taught that an alpha-carboxylate blocks biotinidase cleavage of biotinamide bonds by the Rosebrough paper when it did not teach me, an expert in this area that knows of the need for biotinidase blockade.

6. While the data obtained in the Rosebrough studies were, once my application has been read, suggestive that the carboxylate in the cysteine linker may play a role in blocking biotinidase cleavage, this was not proven in the study. The study showed that a biotin-cysteine-deferoxamine conjugate had 87% stability towards biotinidase cleavage, and that a biotin-desaminolysyl-deferoxamine conjugate without a linker had 45% stability. Based on this data one cannot say with certainty that the alpha-carboxylate was responsible for the higher biotinidase stability. The reason is that the results did not answer the question as to whether the biotinidase stability was due to the cysteine linker or came about by having a combination of the cysteine linker and the desferoxamine. Moreover, one could not predict success from the data. The stability of the biotin-desferoxamine adduct itself suggests that there may be something about the desferoxamine that hinders biotinidase cleavage of the biotinamide bond.

7. I certainly was aware of and read the Rosebrough paper, yet found it necessary to conduct further studies to determine if functional groups alpha to the biotinamide would

block cleavage by biotinidase. Those studies which were subsequently reported by me in 2001 (*Bioconjugate Chem.* 12, 6160623, 2001) demonstrated that a number of functional groups alpha to the biotinamide bond will block biotinidase. My subsequent studies on biotinidase would not have been conducted if I had already been taught that an alpha-carboxylate by itself would block biotinidase activity. Therefore, one of skill in the art could not have assumed that the increased stability was due to the insertion of an alpha carboxylate.

8. Even if others skilled in the arts had made the assumption (but had not been taught) that an alpha-carboxylate was responsible for blocking biotinidase cleavage of biotinamide bonds, and had been taught that an N-methyl blocked biotinidase cleavage from my paper, the combination of this knowledge would not adequately teach or suggest the claimed invention. The reason for this statement is that there are two very important and interactive factors in the biotin derivatives for application to a device to remove toxic materials from the blood, and this information is not taught from the literature. One of the factors is the requirement for very high biotinidase stability. The second factor is that biotin derivatives used must retain a very high binding affinity. The stability toward biotinidase cleavage is critical, but it is also essential in the claimed invention that the high binding affinity of the biotin with avidin or streptavidin be retained. For the purpose of using the products of the present invention, the presence of endogenous biotin in serum makes it essential that a high binding affinity be retained so that the biotin conjugate is not displaced from the column by endogenous biotin. Information on how biotin binding with avidin and streptavidin was affected for various modifications of biotin conjugates was not taught from the literature. Our later studies established a method for determining the relative binding of biotin conjugates (reported in *Bioconjugate Chemistry* 11, 584-598, 2000) and a large number of

biotin derivatives were evaluated to understand how the various modifications affected binding (reported in *Bioconjugate Chemistry* 11, 569-583, 2000). The claimed invention includes these two very important functional aspects.

9. Accordingly, it is my opinion that none of the cited documents, when taken alone or combined, teach or fairly suggest the claimed invention. Moreover, the teachings of the cited documents fail to teach or fairly suggest that in using the products of the invention, a specific combination of molecular functional groups are required to attain efficient trapping of toxic materials and to retain those materials during the process of blood cleansing. In fact, it should be noted that the biotin compound in Wilbur (WO 97/29114) was designed for another application, and without the teaching of the specific requirements for biotinidase blockage and retention of high binding affinity, teaches away from the claimed invention.

10. I declare, under penalty of the perjury laws of the United States, that all statements made herein of my own knowledge are true and that all statements made based on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Respectfully submitted,

By : D. Scott Wilbur

Date Signed : 8/25/04



CURRICULUM VITAE

of

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Personal Data:

Born in Bath, New York - March 18, 1950
Married, one child

Education:

Chemistry Major - Eastern Oregon State College, LaGrande, Oregon;
January 1969 to June 1971

B.S. in Chemistry - (1974) Portland State University, Portland, Oregon;
September 1971 to December 1973

Post-Baccalaureate studies in Chemistry - Portland State Univ.;
January 1974 to June 1974

Ph. D. in Chemistry - (1978) University of California, Irvine, Calif.;
September 1974 to September 1978.

Thesis Advisor - Professor Harold W. Moore.

Thesis; Part I. An Investigation of the Mechanism of Ketene Dimerizations.
Part II. Synthesis of Azepindiones.

Post-doctoral studies in Chemistry - University of California, Irvine, California
September 1978 to December 1978

Professional Experience:

Professor, 7/02 - present
Director, Radiochemistry Division
Associate Professor, 3/90 - 6/02
Department of Radiation Oncology, 356043
University of Washington Medical Center
Seattle, WA 98195

Professional Experience (cont'd):

Director, Radiopharmaceutical Chemistry, 9/86 to 3/90
Head, Radiopharmaceutical Chemistry, 7/86 to 9/86
Head, Radiochemistry, 9/85 to 7/86
Head, Organic Chemistry, 9/84 to 9/85
Senior Scientist, 9/84 to 2/90
NeoRx Corporation
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Affiliate Associate Professor 1985 to 1990
Department of Radiology
University of Washington School of Medicine
University of Washington
Seattle, Washington 98195

Staff Research Chemist, November 1978 to August 1984
Medical Radioisotope Research (INC-3)
Los Alamos National Laboratory
Los Alamos, New Mexico 87545

Adjunct Professor, Chemistry, August 1981 to May 1982
University of New Mexico, Los Alamos Branch
1333 40th Street
Los Alamos, New Mexico 87544

Research Assistant, June 1975 to June 1978
Teaching Assistant, September 1974 to June 1975
Department of Chemistry
University of California, Irvine
Irvine, California 92717

Research Technician, December 1973 to September 1974
Department of Chemistry
Oregon Graduate Center
Beaverton, Oregon

Professional Membership:

American Chemical Society, Organic Chemistry Section, Medicinal Chemistry Section
Society of Nuclear Medicine, Radiopharmaceutical Science Council
American Association for Cancer Research
Society of Radiopharmaceutical Chemistry and Biology

Reviewer of Manuscripts for: *Journal of Nuclear Medicine*, *Bioconjugate Chemistry*,
Journal of Organic Chemistry, *Journal of Medicinal Chemistry*,
Journal of Inorganic Chemistry, *Applied Radiation and Isotopes*,
Nuclear Medicine and Biology, *Cancer Research*, *Chemical Reviews*,
J. Labelled Compounds and Radiopharmaceuticals, *Lancet*,
Mayo Clinic Proceedings, *Carbohydrate Research*

Professional Activities:

Research Peer Review Committee– American Heart Association, Washington Affiliate,
1988, 1989

American Chemical Society

Editorial Advisory Board – *Bioconjugate Chemistry*, American Chemical Society,
1990– present

Reviewer for ACS – Petroleum Research Fund – March 2002

National Institutes of Health

Reviewer for NIH – Radiation Study Section – Outside Reviewer –
Feb. 1991; Nov. 1992; Feb. 1993; Feb. 1994, Nov. 2000

Reviewer for NIH – Diagnostic Radiology Study Section – Outside Reviewer – May 1998

Reviewer for NIH – Experimental Therapeutics–2, Study Section
April 1993 – Special Emphasis Panel.

Reviewer for NIH – Radiation Study Section – Special Emphasis Panel Member
July 2001, January 2002

Reviewer for NIH – SBIR – Phase II – Special Emphasis Panel Member
July 1996

Reviewer for NIH – NCI Site visit team for P01 – Univ. of Tennessee
February 2001

Reviewer for NIH – NCI PO1 review – Rockville, MD
June 2004

Department of Energy

Reviewer for DOE – Feb. 1992 – Site visit team – Review of programs at Brookhaven
National Laboratory
– April 1992 – Review of Nuclear Medicine Research
Los Angeles, CA
– October 1999 – Review of BNCT / Radiopharmaceutical Programs
Washington, D.C.

Reviewer for DOE – Reviewer of Grant Applications; 1990, 1991, 1992, 1994, 1995,
1996, 1998, 1999, 2000, 2001, 2002
SBIR/STTR Program – May 1994, 1996, 1998, 1999, 2000, 2001

Society of Nuclear Medicine:

Scientific Program Committee: Subchairman – Radiopharmaceutical Chemistry
1982, 1985

Reviewer of Abstracts for Society of Nuclear Medicine Annual Meeting:
1982, 1984, 1985, 1986, 1987, 1989, 1991, 1995, 2001, 2002,
2003, 2004

Secretary-Treasurer for Radiopharmaceutical Science Council –
1990/1991

President-Elect of Radiopharmaceutical Science Council of the Society of Nuclear Medicine –
June 2000–June 2002

President of Radiopharmaceutical Science Council of the Society of Nuclear Medicine –
June 2002–June 2004

Past-President of Radiopharmaceutical Sciences Council of the Society of Nuclear Medicine –
June 2004–2005

Member of SNM House of Delegates; June 2002 –

Member of Committee on Councils; June 2002 –

Member of Task Group on SNM Website; June 2001 – 2003

Member of Task force on a National Radionuclide Production Facility; May 2003 –

Member of Committee on Radiopharmaceuticals, June 2003–

Professional Activities (cont'd):

Symposia Organization

- Organizing Committee member for Third International Symposium on Radiohalogens held Sept. 20-23, 1992, Banff, Alberta, Canada
- Scientific Program Committee member for Ninth International Symposium of Radiopharmacology held in Ann Arbor, Michigan on June 7-10, 1995; Chairman for Session on Boron Neutron Capture Therapy
- Organizing Committee member for 11th International Symposium on Radiopharmaceutical Chemistry held in Vancouver, BC August 14-18, 1995; Reviewer of Abstracts for Meeting; Moderator of Session on Radiolabeling Antibodies, Peptides and Proteins
- Chairman and Organizer of Session on "Isotopes in Macromolecules: Protein, Nucleic Acid, and Monoclonal Antibody Research" in the 6th International Symposium on the Synthesis and Applications of Isotopes and Labeled Compounds held Sept. 1997, Philadelphia, PA.
- Chairman and Organizer of Session III: "Labeling with Alpha-Emitters and Carrier Optimization" in the Second Bi-annual Workshop on Alpha-Emitters in Medical Therapy held in Toronto, Canada, June 4-5, 1998.
- Organizing Committee member for Fourth International Symposium on Radiohalogens held Sept. 9-14, 2000, Whistler, British Columbia, Canada
- Co-Organizer of Symposium: Development of High LET Therapeutic Radiopharmaceuticals" held at the American Chemical Society meeting in March 2003.
- Organizing Committee member for Fifth International Symposium on Radiohalogens to be held Sept. 2004, Whistler, British Columbia, Canada

University of Washington:

Standing Committee for Cancer Institutional Grants in the UW School of Medicine
2000, 2001

Inventor on Patents Issued:

1. D.S. Wilbur and S.W. Hadley: Vinyl Substituted Radiohalogen Conjugates for Protein Labeling. Patent Number 4,870,188; Issued Sept. 26, 1989.
2. D.S. Wilbur and S.W. Hadley: Vinyl Substituted Radiohalogen and Methods of Use Conjugates. Patent Number 4,876,081; Issued Oct. 24, 1989.
3. J.M. Reno, B.J. Bottino, and D.S. Wilbur: Radionuclide Antibody Coupling. Patent Number 4,877,868; Issued Oct. 31, 1989.
4. D.S. Wilbur, A.R. Fritzberg, and D.S. Jones: Radiohalogenated Proteins. Patent Number 4,885,153; Issued Dec. 5, 1989.
5. A.R. Fritzberg, S. Kasina, A. Srinivasan, and D.S. Wilbur: Metal Radionuclide Labeled Proteins for Diagnosis and Therapy. Patent Number 4,897,255; Issued Jan. 30, 1990.
6. A.R. Fritzberg, S. Kasina, A. Srinivasan, D.S. Wilbur: Metal Radionuclide Labeled Proteins for Diagnosis and Therapy. Patent Number 5,037,630; Issued Aug. 6, 1991.
7. D.S. Wilbur and A.R. Fritzberg: Radiohalogenated small molecules for protein labeling. Patent Number 5,045,303; Issued Sept. 3, 1991.
8. D.S. Wilbur: Modified Cellular Substrates Used As Linkers For Increased Cell Retention of Diagnostic and Therapeutic Agents. Patent Number 5,057,301; Issued Oct. 15, 1991.
9. A.R. Fritzberg, D.S. Wilbur, A. Srinivasan, and D. W. Wester: Minimal derivatization of proteins. Patent Number 5,059,541; Issued Oct. 22, 1991.
10. D.S. Wilbur and S.W. Hadley: Process for Isolation and Radiolabeling of Pharmaceuticals with Isotopes of Astatine. Patent Number 5,102,651, Issued April 7, 1992.

11. A.R. Fritzberg, S. Kasina, A. Srinivasan, and D.S. Wilbur: Method of Producing Metal Radionuclide Labeled Proteins for Diagnosis and Therapy. Patent Number 5,120,526, Issued June 9, 1992.
12. A.R. Fritzberg, S. Kasina, a. Srinivasan, and D.S. Wilbur: Metal Radionuclide Labeled Proteins for Diagnosis and Therapy. Patent Number 5,175,343, Issued December 29, 1992.
13. D.S. Wilbur and S.W. Hadley: Vinyl substituted radiohalogen conjugates for protein labeling. Patent Number 5,200,169, Issued April 6, 1993.
14. D.S. Wilbur and A.R. Fritzberg: Radiohalogenated small molecules for protein labeling. Patent Number 5,213,787, Issued May 25, 1993.
15. A.R. Fritzberg, S. Kasina, A. Srinivasan, and D.S. Wilbur: Metal Radionuclide labeled proteins for diagnosis and therapy. Patent Number 5,242,679; Issued Sept. 7, 1993.
16. D.S. Wilbur: Iodinated Borane Cage Molecules as X-Ray Contrast Media. Patent Number 5,489,673; Issued February 6, 1996.
17. D.S. Wilbur and A.R. Fritzberg: Radiohalogenated small molecules for protein labeling. Patent Number 5,609,848; Issued March 11, 1997.
18. D.S. Wilbur: Iodinated Borane Cage Molecules as X-Ray Contrast Media. Patent Number 5,679,322; Issued October 21, 1997.
19. D. S. Wilbur, P.M. Pathare, and A.C. Morgan Jr.: Biotinylated Cobalamins. Patent Number 5,739,287; Issued April 14, 1998.
20. A.C. Morgan, D.S. Wilbur, and P.M. Pathare: Vitamin B12 Receptor Modulating Agents and Methods Related Thereto. April 24, 1997, WO97/14711, US Patent Number 5,840,712; issued November 24, 1998.
21. A.C. Morgan and D.S. Wilbur: Receptor Modulating Agents, US Patent Number 5,840,880; issued November 24, 1998.
22. AC. Morgan and D.S. Wilbur: Methods of receptor modulation and uses thereof. US Patent Number 5,869,465, issued February 9, 1999.
23. A.C. Morgan, D.S. Wilbur, and P.M. Pathare: Water soluble vitamin B₁₂ receptor modulating agents and methods related thereto. US Patent Number 6,083,926, issued July 4, 2000.
24. D.S. Wilbur and P.M. Pathare: Discrete-Length Polyethylene Glycols. US Patent number 6294697, issued September 25, 2001.
25. D.S. Wilbur and P.M. Pathare: Discrete-Length Polyethylene Glycols (Continuation). US Patent number 6,492,560, issued December 10, 2002

Inventor on Patents Pending and Published as PCT:

26. D.S. Wilbur, P.M. Pathare, S.A. Weerawarna, and D.K. Hamlin: Biotin-Containing Compounds, Biotinylation Reagents and Methods. August 14, 1997, WO 97/29114.
27. D.S. Wilbur, P.M. Pathare, and D.K. Hamlin: Water-Soluble Multi-Biotin-Containing Compounds. US Appl. 09/324,267.
28. D.S. Wilbur, P.M. Pathare, and D.K. Hamlin: Water-Soluble Multi-Biotin-Containing Compounds (Continuation-in-part). US Appl. 10/261.060.
29. D.S. Wilbur and B.E.B. Sandberg: Reagent for conjugation to a biomolecule. PCT/SE98/01345 and PCT/SE99/01241.
30. D.S. Wilbur and B.E.B. Sandberg: Trifunctional reagent for conjugation to a biomolecule. US Application September 20, 2001, 20010023288.
31. B.E.B Sandberg, D.S. Wilbur, and R. Nilsson: Biotin Derivatives. June 15, 2001, US Appl. 09/881.213.

Co-Inventor on additional pending patent applications.

Funding from Contracts and Grants:

- Principal Investigator on Small Business Innovative Research Contract entitled "Radioiodinated Conjugates for Therapy and Diagnosis" Phase I (N43-CM-57759) – October 1985 to April 1986 Phase II (N43-CM-67759)– October 1986 to Sept. 1988
- Principal Investigator on Small Business Innovative Research Contract entitled "Astatine-211 Labeled Antibodies for Therapy" Phase I (N43-CM-67939) – October 1986 to April 1987
- Principal Investigator on Biological Research Support Grant (BRSG – from NIH) entitled: "Modification of Monoclonal Antibodies for Site-Specific Attachment of Therapeutic Agents." March 1991 to March 1992
- Principal Investigator on research contract with Merck, Sharp & Dohme Research Laboratories entitled "Synthesis and Radioiodination of Phenylalanine Derivatives" December 1991 to November 1992
- Principal Investigator on research contract with Mallinckrodt Medical, Inc. entitled "Development of Highly Iodinated Molecules as X-Ray Contrast Agents" – April 1992 to December 1994.
- Principal Investigator on research contract with NeoRx Corporation entitled "Astatine-211 labeled Monoclonal Antibodies" December 1992 to December 1993.
- Principal Investigator on research contract with Receptagen, Inc. entitled "Modification of Vitamin B₁₂ and Assessment of Biological Activity" – May 1993 to September 1998.
- Principal Investigator on research contract with Receptagen, Inc. entitled "Structural Modification of a Coenzyme for Application to Medicine" – October 1993 to September 1996.
- Principal Investigator on DOE Funded Research entitled "Dimeric scFv antibodies and Their Streptavidin/Biotin Conjugates in Cancer Imaging and Therapy" – May 1995 to February 1998.
- Principal Investigator on research contract with Bracco s.p.a., Milan, Italy, entitled "Preparation of Highly Iodinated Boranes" – March to May, 1996.
- Principal Investigator on research contract with Battelle Pacific Northwest National Laboratory, entitled "Development of Linker Chemistry for Radium Chelates" – May-Sept. 1997.
- Principal Investigator (Co-Principal with Dr. Rainer Storb, FHCRC) on research grant from The Rich Foundation, Luzern Switzerland entitled "Radioimmunotherapy with Alpha-Emitting Radionuclides as a Novel Conditioning Program for Marrow Transplantation" – February 1998 – January 2001.
- Co-Investigator (Principal Investigator is Dr. Oliver Press) on NIH supported grant entitled "Pretargeting of Radioimmunotherapy of CD20+ Lymphomas" – January 1998 thru June 2002.
- Principal Investigator on DOE Funded Research entitled "Development of Biotin/Streptavidin Reagents for Antibody Pretargeting of Cancer – March 1998 to February 2001.
- Principal Investigator on DOD Funded Research entitled "Preclinical Evaluation of a Targeted Alpha-Emitting Radionuclide in Radiotherapy of Breast Cancer" – April 1998 to March 2000.
- Principal Investigator on Contract from Moss, Inc. entitled "Synthesis of a Novel Biotin Compound". January 1998 to March 1998.
- Principal Investigator on DOD Funded Research entitled "Pretargeting of Astatine-211 for Therapy of Metastatic Prostate Cancer". July 1998 – August 2001.
- Principal Investigator on Contract from Mitra Medical Technologies entitled "Development of Reagents for a Tag-Kit". November 1998 – July 2004.
- Principal Investigator on DOE Funded Research entitled "Evaluation of Reagents for Rapid and Stable Labeling of Biomolecules with Astatine-211". Nov. 2000 – October 2003.
- Principal Investigator on DOE Funded Research entitled "Development of Reagents for Application of At-211 and Bi-213 to Targeted Radiotherapy of Cancer". Mar. 2001 – Feb. 2005.
- Principal Investigator for subcontract for NIH grant (FHCRC), Principal Investigator Dr. Oliver Press, "Radioimmunotherapy of B-Cell Lymphomas using Pretargeting Approaches" – July 2002 thru June 2006.
- Principal Investigator on subcontract for NIH grant (FHCRC) Principal Investigator Dr. Brenda Sandmaier, Nonmyeloablative Grafts: Haploidentical Littermate Dogs", July 2002 thru June 2004.

Funding from Contracts and Grants (Cont'd)

Principal Investigator on DOD funded research entitled "In Vitro Assessment of a Peptide Nucleic Acid (PNA)-Peptide Conjugate Labeled with an Auger-Emitting Radionuclide for Prostate Cell Killing". Feb 2004-Feb 2005.

Principal Investigator on DOE funded support for a conference; "Fifth International Symposium on Radiohalogens, September 11-15, 2005

Publications in Peer Reviewed Journals:

1. Wilbur D.S. and Moore H.W. (1978) Cyanoketenes. Mechanism of *tert*-Butylcyanoketene Cycloaddition to Methyl- and Ketoketenes. *J. Amer. Chem. Soc.* 100, 6523-6525.
2. Moore H.W. and Wilbur D.S. (1980) Cyanoketenes. Mechanism of *tert*-Butylcyanoketene Cycloaddition to Aldo- and Ketoketenes. *J. Org. Chem.* 45, 4482-4491.
3. Wilbur D.S., Bentley G.E. and O'Brien H.A., Jr. (1981) A Rapid Synthesis of A-Ring Bromine-77-Labeled Estrogens with High Specific Activity. *J. Label. Compds. Radiopharm.* 18, 1693-1701.
4. Wilbur D.S. and Anderson K.W. (1982) Bromine Chloride from N-Chlorosuccinimide Oxidation of Bromide Ion. Electrophilic Addition Reactions in Protic and Aprotic Solvents. *J. Org. Chem.* 47, 358-359.
5. Wilbur D.S. and O'Brien H.A., Jr. (1982) A-Ring Bromination of Estradiol and 17 α -Ethinylestradiol with N-Chlorosuccinimide and Bromide Ion. *J. Org. Chem.* 47, 359-362.
6. Wilbur D.S., Anderson K.W., Stone W.E. and O'Brien H.A., Jr. (1982) Radiohalogenation of Non-activated Aromatic Compounds Via Aryltrimethylsilyl Intermediates. *J. Labelled Compds. Radiopharm.* 19, 1171-1187.
7. Gibson R.E., Eckelman W.C., Francis B., O'Brien H.A., Mazaitis J.K., Wilbur D.S., and Reba R.C. (1982) [Br-77]-17 α -Bromoestradiol *In Vivo* and *In Vitro* Characterization of an Estrogen Receptor Radiotracer. *Int. J. Nucl. Med. Biol.* 9, 245-250.
8. Wilbur D.S., Stone W.E. and Anderson K.W. (1983) Regiospecific Incorporation of Bromine and Iodine into Phenols Using Trimethylsilylphenol Derivatives. *J. Org. Chem.* 48, 1542-1544.
9. Hylarides M.D. and Wilbur D.S. (1983) B-Ring Aromatization of Estrogen Derivatives. *Steroids* 41, 657-662.
10. Wilbur D.S. and Svitra Z.V. (1983) Organopentafluorosilicates. Reagents for Rapid and Efficient Incorporation of No-Carrier-Added Radiobromine and Radioiodine. *J. Labelled Compds. Radiopharm.* 20, 619-626.
11. Wilbur D.S. (1984) Structural Determination of Some Chloroazepin-2,5-diones Using a Lanthanide Shift Reagent. *J. Heterocycl. Chem.* 21, 801-807.
12. Cromer D.T., Ryan R.R. and Wilbur D.S. (1984) Structure of 1-H-Azepine-2-One-5-Methoxime, C₇H₈N₂O₂. *Acta Cryst.* C40, 301-303.
13. Wilbur D.S. and Svitra Z.V. (1984) Electrophilic Radiobrominations of Hippuric Acid: An Example of the Utility of Aryltrimethylsilane Intermediates. *J. Label. Compds. Radiopharm.* 21, 415-428.
14. Wilbur D.S., Garcia S.R., Adam M.J. and Ruth T.J. (1984) An Evaluation of the Introduction of Stable Nuclides of Bromine into High Specific Activity Radiobrominations. *J. Labelled Compds. Radiopharm.* 21, 767-779.
15. Hylarides M.D., Leon A.A., Mettler F.A., and Wilbur D.S. (1984) Synthesis of 1-Bromoestradiol. *J. Org. Chem.* 49, 2744-2745.
16. Hylarides M.D., Buksa P.L., Mettler F.A. and Wilbur D.S. (1985) Radiobromination of the 1-position of Estradiol Using No-Carrier-Added Bromine-77. *J. Labelled Compds. Radiopharm.* 22, 437-441.
17. Hylarides M.D., Leon A.A., Mettler F.A. and Wilbur D.S. (1985) Radiolabeling of B- and C-Ring of Estradiol Using No-Carrier-Added Bromine-77. *J. Labelled Compds. Radiopharm.* 22, 443-450.

18. Speranza M., Shiue C.Y., Wolf A.P., Wilbur D.S. and Angelini G. (1984) Regiospecific Radiofluorination of Arylpentafluorosilicates as a General Route to F-18-Labelled Arylfluorides. *J. Chem. Soc. Chem. Commun.* 1448-1449.
19. Speranza M., Shiue C.Y., Wolf A.P., Wilbur D.S. and Angelini G. (1985) Electrophilic Radiofluorination of Aryltrimethylsilanes as a General Route to F-18 Labelled Arylfluorides. *J. Fluorine Chem.* 30, 97-107.
20. Grunbaum Z., Freau S.J., Krohn K.A., Wilbur D.S., Magee S. and Rasey J.S. (1987) Synthesis and Characterization of Congeners of Misonidazole for Imaging Hypoxia. *J. Nucl. Med.* 28, 68-75.
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